HIGHLY SUBSTITUTED CYCLOHEPTATRIENE DERIVATIVES

by

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A MASTER'S THESIS

submitted in partial fulfillment of the

requirements for the degree

MASTER OF SCIENCE

Department of Chemistry

KANSAS STATE UNIVERSITY
Manhattan, Kansas

1967

Approved by:

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Major Professor

ACKNOWLEDGMENT

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The compound tropilidene was first synthesized by Ladenburg[1] in 1881 from the alkaloid tropine. There were several early attempts at structure formulation. Merling[2] proposed a six-membered ring with an exocyclic methylene (I). It was found that tropilidene added one mole of bromine and on heating gave hydrogen bromide and benzyl bromide. Einhorn and Willstater[3] proposed the bicyclic structure (II) but later abandoned it because a hydrocarbon of that structure was found and had different chemical and physical properties. In 1901 Willstater[4] repeated Ladenburg's synthesis

Figure 1. Structures proposed for tropilidene.

and also prepared tropilidene by several other methods starting from cycloheptene. Several structures were considered by Willstater for tropilidene (III, IV, and V). Structure IV was rejected because tropilidene absorbed three moles of hydrogen to give cycloheptane, and there was no reason to assume that this structure would do this. Also there was no apparent way of explaining how such a structure could be formed in the course of the syntheses. Recently a compound with this structure was prepared[5] by photoisomerization of tropilidene, and its properties are quite different from tropilidene. Structure III was rejected because no cyclopropane-1,2-dicarboxylic acid was found on permanganate oxidation, and the bicyclic system was supposed to be subject to labile rearrangement to the cycloheptatriene system. It was concluded, therefore, that tropilidene had the structure V, 1,3,5-cycloheptatriene.

In 1954 Doering and Knox[6] found that tropilidene could be synthesized from benzene and diazomethane by photochemical addition. More recently, similar syntheses for tropilidene and its derivatives have been discovered[7-13]. Since this type of addition to a double bond results in the formation of a cyclopropane ring, it was reasoned that structure III was a possibility. Chemical evidence for this is found in reactions which give norcaradiene derivatives as a product[14-19]. For example, tropilidene reacts with maleic anhydride in boiling xylene to give the Diels-Alder adduct (VI).

Corey, Burke, and Remers[20] examined the NMR spectra for a series of enol esters of eucarvone (VII). The absence of absorption in the region expected for the two tertiary bridge hydrogens in norcaradiene, and the agreement of the spectra with that expected for cycloheptatriene allowed elimination of the bicyclic structure for these compounds. However, low temperature ozonolysis of these esters gave large amounts of cis-caronic acid.
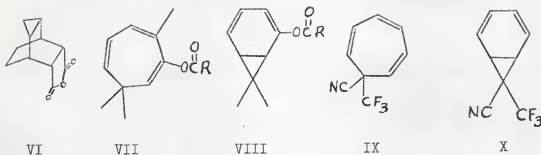

Figure 2. Structures reported for some tropilidene derivatives.

Ciganek[21] has reported that the adduct of cyanotrifluoromethylene carbene to benzene is, at room temperature, a rapidly equilibrating mixture of 7-cyano-7-trifluoromethyl-1,3,5-cycloheptatriene (IX) and 7-cyano-7-trifluoromethylnorcaradiene (X). NMR data shows two species in rapid

equilibrium at room temperature. The major component of the mixture was reported to be IX. The low energy of activation suggested that the two components are simply valence tautomers.

Recently, stable norcaradiene derivatives have been obtained by placing a three carbon bridge between C-1 and C-6 or by incorporating a double bond into an aromatic system. Ciganek[22] prepared 7,7-dicyano-norcaradiene, and NMR data[22,23] indicated that it has the bicyclic structure. In attempting to synthesize 7,7-dicyano-2,3-benzonorcaradiene (XI), Ciganek isolated in addition to the desired material the cycloheptatriene derivatives XII and XIII. These three compounds proved to be good models for comparison of the NMR spectra of the valence tautomers. In the norcaradiene structure the tertiary bridge protons absorbed at 6.20 and 6.65 , while in the cycloheptatriene structures the absorption was at about 4 .

Huisgen and Juppe[24] found that 2,3-benzonorcaradiene-7-carboxylic acid gave spectral data consistent with the bicyclic structure XIV. Vogel
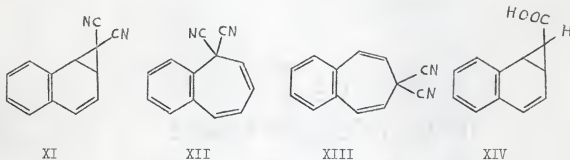

Figure 3. Norcaradiene-tropilidene tautomers.

and coworkers[25] and Eschenmoser and coworkers[26] have prepared stable norcaradiene compounds with C-1 to C-6 bridges (XV[25] and XVI[26]). Maier[27] prepared a nitrogen analog of the norcaradiene derivatives (XVII) and used NMR to determine the bicyclic structure.

The degree of planarity of cycloheptatriene and its derivatives has in recent years been the subject of much discussion. Doering and coworkers[18] proposed the possibility that instead of a valence tautomeric mixture, tropilidene exists in a "pseudoaromatic" structure (XVIII). The 1,6-orbital overlap would produce a six -electron, closed, aromatic-like system. The situation is analogous to conjugation in homoallylic or homoaromatic systems. Evans and Lord[28] agreed with this structure assignment and assigned infrared and Raman frequencies on the basis of a structure of C_{2v} symmetry.

Conn, Kistiakowsky, and Smith[29] reported a resonance energy of 6.7 kcal which suggests a triene in which no 1,6-overlap occurs. Turner and coworkers[30] verified this resonance energy but attributed the low value to underestimation of the strain energy involved in making the molecule planar for the pseudo-aromatic structure. Conrow[31] reported that the 1,6-overlap should contribute only about 1.3 kcal to the total resonance energy of the molecule. This low value is in agreement with the work of Davis and Tulinsky[32]. The configuration of 7,7-dimethylcycloheptatriene-3-carboxylic acid as determined by x-ray studies allowed the possibility that some 1,6-overlap could occur. However, these authors suggested that the overlap occurs only below and not above the molecule giving rise to a "half -bond."
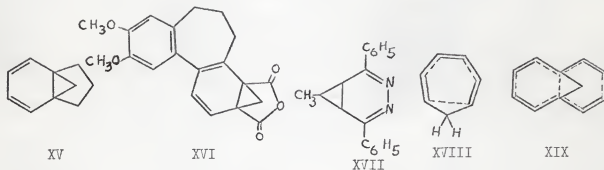

Figure 4. Stable norcaradiene structures.

Vogel and Roth[33] have reported a naphthalene derivative (XIX) which shows definite aromatic character. The compound has a high resonance energy, and the NMR spectrum shows an A_2B_2 system for eight protons at 2.5-3.2 δ (center at 2.8 δ). This suggests the definite possibility of 1,6-overlap and is in agreement with Doering's proposal.

Recent electron diffraction and x-ray studies have shown that tropilidene is not planar and therefore is not likely to have a pseudo-aromatic structure. Dunitz and Pauling[34] found that cycloheptatriene molybdenum tricarbonyl, $C_7H_8Mo(CO)_3$, has a structure with carbon atoms 1 through 6 coplanar and carbon-7 0.67 Å. out of plane. Davis and Tulinsky[32] reported that in 7,7-dimethyl-cycloheptatriene-3-carboxylic acid, carbon atoms 1,2,5 and 6 are coplanar, carbon-7 is 0.63 Å. out of plane and atoms 3 and 4 are 0.48 Å. out of plane. The molecule is in a boat configuration. Traetteberg[35] and Butler[36] have reported similar structures for cycloheptatriene (Figure 1).

Infrared[37] and NMR spectral data has confirmed that the molecule is in a non-planar boat configuration. The NMR spectra show that the molecule is rapidly inverting. The rate of inversion is extremely fast even at very low temperature. For cycloheptatriene[38] at about -150° C., the methylene protons give rise to two distinct bands with a separation of 76 c.p.s. This separation was found to increase with decrease in temperature. The rate of inversion at this temperature was 55 sec^{-1}. The free energy of activation for inversion was calculated to be 6.1 kcal. A similar spectrum was obtained[39] for 7-deuterocycloheptatriene. The bulkier molecule, 2-t-butyl-3,7,7-trimethyl-1,3,5-cycloheptatriene[40], appeared to have a much slower rate of inversion. The gem-dimethyl groups became nonequivalent at about -100° C. Anet[38] calculated a free energy of inversion of 9.2 kcal. for the bulky molecule.

EXPLANATION OF PLATE I

Fig. 5.   Non-planar tropilidene structure.

Fig. 6.   Pentasubstituted tropilidenes.
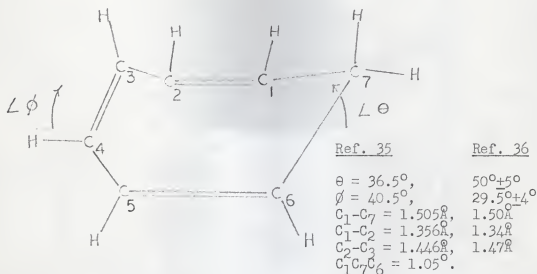
PLATE I

∠ φ

∠ θ

Ref. 35	Ref. 36
θ = 36.5°,	50°±5°
φ = 40.5°,	29.5°±4°
C_1-C_7 = 1.505Å,	1.50Å
C_1-C_2 = 1.356Å,	1.34Å
C_2-C_3 = 1.446Å,	1.47Å
$C_1C_7C_6$ = 1.05°.	

Fig. 5

XXa) R=CH_3-, R'=$(CH_3)_3C$-
 b) R=CH_3CH_2-, R'=$(CH_3)_3C$-
 c) R=$(CH_3)_2CH$-, R'=$(CH_3)_3C$-
 d) R=R'=$(CH_3)_3C$-
 e) R=CH_3-, R'=$(CH_3)_2CH$-
 f) R=$(CH_3)_3C$-, R'=$(CH_3)_2CH$-
 g) R=R'=$(CH_3)_2CH$-
 h) R=$(CH_3)_3C$-, R'=$(CH_3)_2CH$-

XXIa) R=CH_3-, R'=$(C_6H_5)_3C$-
 b) R=CH_3CH_2-, R'=$(C_6H_5)_3C$-
 c) R=$(CH_3)_2CH$-, R'=$(C_6H_5)_3C$-
 d) R=$(CH_3)_3C$-, R'=$(C_6H_5)_3C$-

XXIIa) R=CH_3-, R'=$(C_6H_5)_3C$-
 b) R=CH_3CH_2-, R'=$(C_6H_5)_3C$-
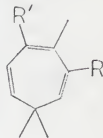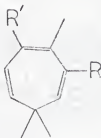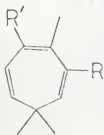
Fig. 6

EXPLANATION OF PLATE II

Fig. 7.   Synthesis of 2,3,4,7,7-pentasubstituted
          tropilidenes.
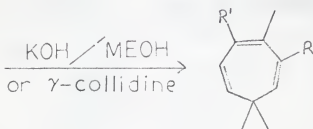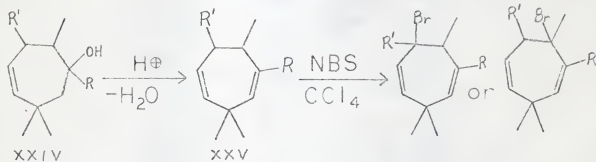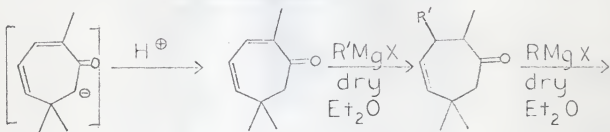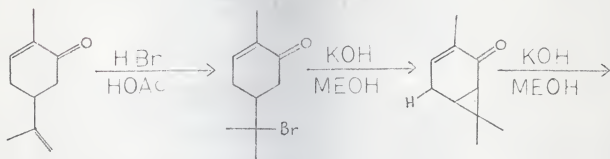
PLATE II

Fig. 7

EXPLANATION OF PLATE III

Fig. 8.   2-Alkylidene-3,7,7-trimethyl-4-alkyl-3,5-
cycloheptadiene.

Fig. 9.   Synthesis of 2,3,5,7,7-pentasubstituted
tropilidenes.

PLATE III
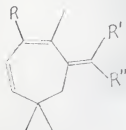
XXIIIa) R=(CH$_3$)$_3$C-, R'=R''=H-
    b) R=(CH$_3$)$_3$C-, R'=H-, R''=CH$_3$-
    c) R=(CH$_3$)$_3$C-, R'=R''=CH$_3$-
    d) R=(CH$_3$)$_2$CH-, R'=R''=H-
    e) R=(CH$_3$)$_2$CH-, R'=H-, R''=CH$_3$-
    f) R=(CH$_3$)$_2$CH-, R'=R''=CH$_3$-

Fig. 8
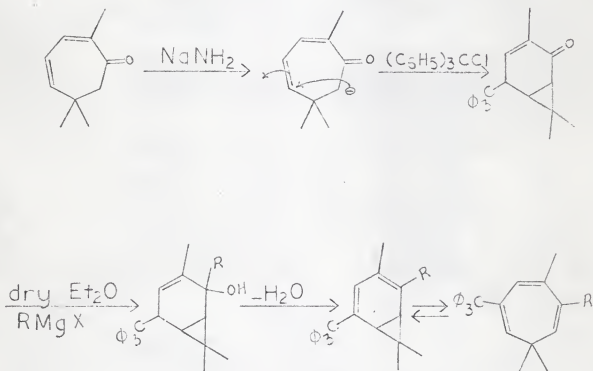
Fig. 9

EXPLANATION OF PLATE IV

Fig. 10.   Synthesis of 2,3,6,7,7-pentasubstituted
           tropilidenes.

Fig. 11.   Mechanism for the formation of
           dieucarvelone.

PLATE IV
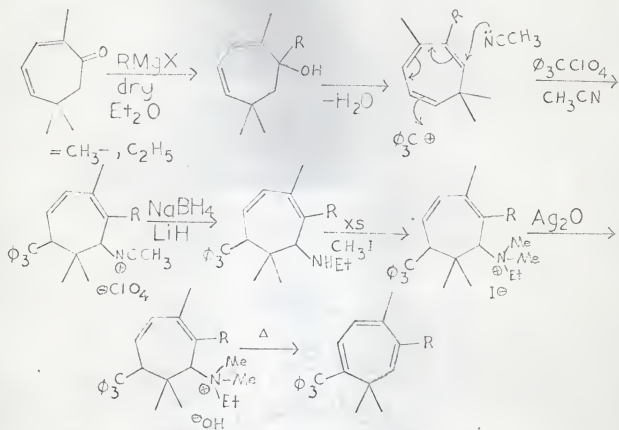
Fig. 10
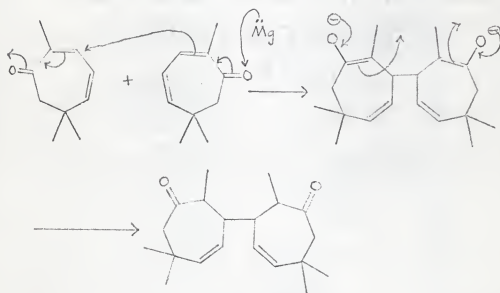
Fig. 11

EXPLANATION OF PLATE V

Fig. 12.   Transannular ether formation.

Fig. 13.   Synthesis of eucarvone enol triphenylmethyl
ether.
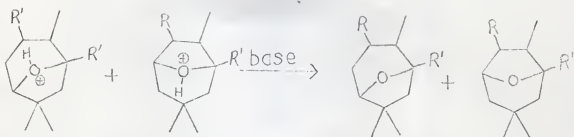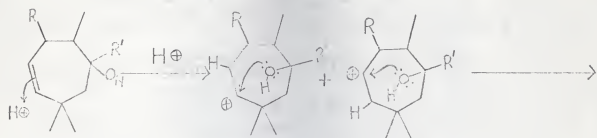
PLATE V

$R = t\text{-}butyl$ or $isopropyl$
$R' = isopropyl$ or $t\text{-}butyl$

Fig. 12
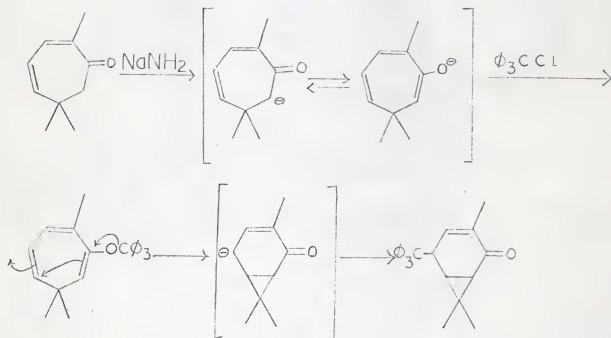
Fig. 13

EXPLANATION OF PLATE VI
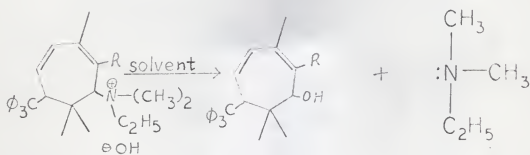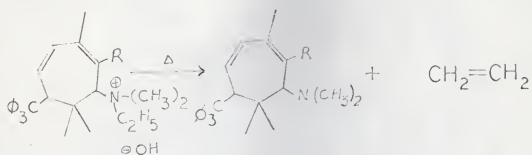
PLATE VI

Fig. 14
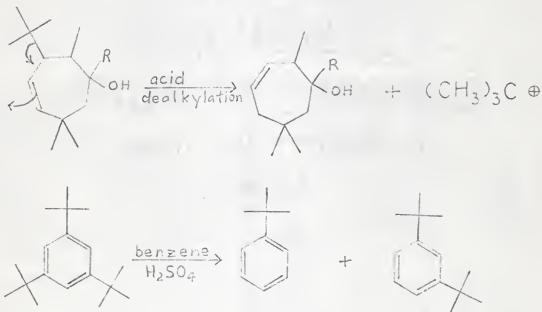
Fig. 15

EXPLANATION OF PLATE VII·

Fig. 16.   The transannular ether from dehydration of
2,6,6-trimethyl-1-isopropyl-3-t-butyl-
cyclohept-4-enol.

Fig. 17.   Dieucarvelone.

Fig. 18.   Eucarvone enol triphenylmethyl ether.

PLATE VII
Figure 16

Wavelength

Figure 17

Wavelength

Figure 18

Wavelength
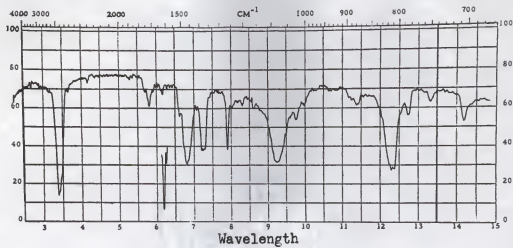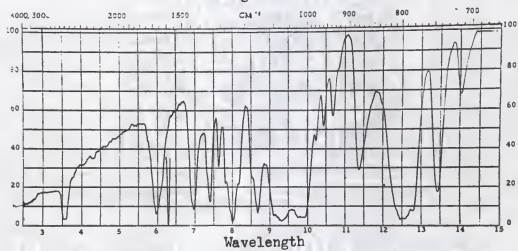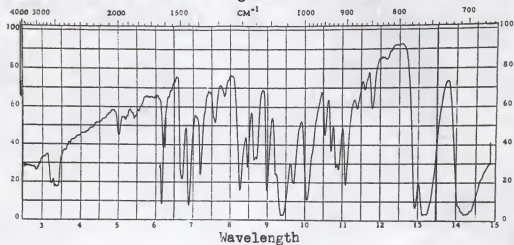
EXPLANATION OF PLATE VIII

Fig. 19.   5-Triphenylmethyl carenone.

Fig. 20.   Triphenylmethyl ethyl ether.

Fig. 21.   3,7,7-Trimethyl-2,4-di-$\underline{t}$-butyl-1,3,5-cycloheptatriene.

PLATE VIII
Figure 19

Figure 20

Wavelength

Figure 21

Wavelength
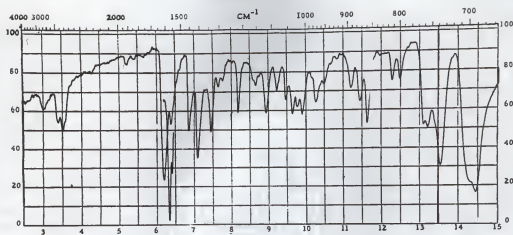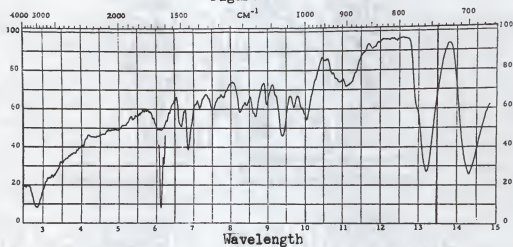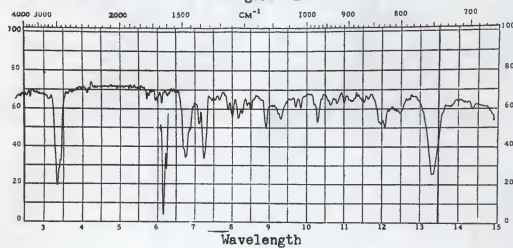
EXPLANATION OF PLATE IX

Fig. 22.   3,7,7-Trimethyl-2-ethyl-3-_t_-butyl-1,3,5-
          cycloheptatriene.

Fig. 23.   N-(5-Triphenylmethyl-1,2,6,6-tetramethyl-
          cycloheptadien-7-yl)-acetonitrilium per-
          chlorate.

Fig. 24.   Ethyl 5-triphenylmethyl-1-ethyl-2,6,6-
          trimethylcycloheptadien-7-yl amine.

PLATE IX

Figure 22

Wavelength

Figure 23

Wavelength

Figure 24

Wavelength
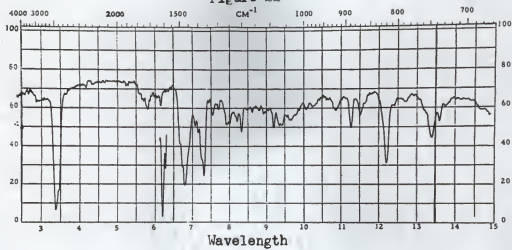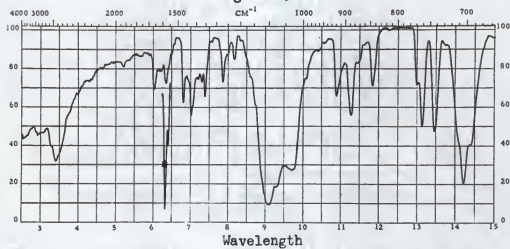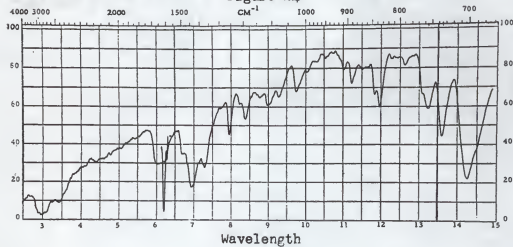
It can be concluded from the work to the present that tropilidene is a non-planar, monocyclic molecule in a rapidly inverting boat configuration. Certain derivatives, however, show deviations from this structure. In some the bicyclic structure appears to be in equilibrium with its tautomer, and in others it may exist independently.

INTRODUCTION:

In view of previous results, it was felt that further work should be done to study the structures involved in the tropilidene ring system. The synthesis of a series of pentaalkyl tropilidenes was attempted to determine the effect of loading the molecule on the planarity of the ring system.

From a study of models, predictions can be made for structures of these compounds. In the 2,3,4,7,7-pentasubstituted tropilidenes (XX), increased steric interaction between the gem-dimethyl group and the subsittuents on carbon atoms 3 and 4 should tend to counteract the effects of decreased bond angle strain and increased 1,6-overlap in the non-planar system and should make the molecule slightly more planar. In the 2,3,5,7,7-pentasubstituted tropilidenes (XXI), the steric interactions are not greatly increased and the planarity should be about the same as for previously reported tetrasubstituted tropilidenes[40]. In 2,3,6,7,7-pentasubstituted tropilidenes (XXII) increased steric interaction between substituents on carbon 6 and 7 should cause an increase in non-planarity.

DISCUSSION OF RESULTS:

The proposed synthetic scheme for the synthesis of the 2,3,4,7,7-pentasubstituted tropilidenes is shown in Figure 3. The starting material was 1-carvone which was converted to eucarvone by the method of Corey and Burke[15]. This is followed by a 1,4-addition of a Grignard reagent, a normal Grignard addition and dehydration of the resulting alcohol. Allylic

bromination and dehydrobromination should give a mixture of isomers XX and
XXIII. Isomer XX should predominate since it is more stable than isomer
XXIII[31] (Figure 8).

The proposed synthetic scheme for the 2,3,5,7,7-pentasubstituted
tropilidenes is shown in Figure 5. The procedure for preparing 3,7,7-
trimethyl-5-triphenylmethylbicyclo[4.1.0] hept-3-en-2-one (XXVII) was that
given by Conrow[46] and Corey and Burke[15]. Conrow originally reported that
this synthesis led to the production of eucarvone enol triphenylmethyl
ether. Doering and Willcott[47] proved the compound to actually be the
bicyclic ketone. A Grignard reaction followed by dehydration is proposed
for this bicyclic ketone.

The proposed synthetic scheme for the 2,3,6,7,7-pentasubstituted
tropilidenes is shown in Figure 6. The 2,3,7,7-tetrasubstituted tropili-
dene is prepared by a Grignard reaction and dehydration. The nitrilium
perchlorate salt is formed by the method described by Conrow[46]. The
nitrilium salt is to be reduced by sodium borohydride. A Hofmann elimina-
tion is proposed for the resulting amine.

Due to the apparently straightforward nature of the syntheses, it was
decided to synthesize a number of compounds so that a series would be avail-
able for investigation of their physical properties. Because a number of
isomers might be formed in the dehydration and allylic bromination steps
which would all react to give the same dehydrobromination products, the
formation of mixtures in the preceding steps was expected, and no attempt was
made to separate or identify the components. It was expected that separation
would be easier and more useful at the completion of the sequence. It was
found that this attack was a poor choice. There is evidence that dehydration

was not always simple but led to some ether formation and rearrangement instead of, or, in addition to, the desired course of reaction. The allylic bromination/dehydrobromination sequence did not proceed as expected either. In certain instances the analysis of the resultant hydrocarbon showed that the desired dehydrogenation had not been effected.

The full proper identification of the products of these reactions was further hindered by the fact that the NMR spectrometer was inoperative when these products were obtained, by the renovation of the building, and by the lack of time due to pressing commitments by the author.

Of the eight 2,3,4,7,7-pentasubstituted tropilidenes whose syntheses were attempted, only five seemed to be formed. The syntheses for compounds XXc,g and h all failed in the dehydration step (Figure 7, XXIV to XXV). No explanation is apparent for this failure since there is no reason not to expect the alcohol to protonate, and once protonation is accomplished there are three positions available for loss of a proton to form the double bond. Also, it was possible to synthesize XXd which is the bulkiest of the molecules in this series and, therefore, should be the most difficult to protonate.

In the attempted dehydration of XX c, g, h using concentrated sulfuric acid and glacial acetic acid, four compounds were obtained in each case in equal quantities which appeared to be isomers from their VPC retention times. Their infrared spectra (Figure 16) indicate that they are ethers. The proposed structures and the mechanism for the formation of these compounds are shown in Figure 6. Elemental analyses gave confirmation for these structures.

Dehydration of XXd was attempted using boric acid as the dehydrating agent. The reaction mixture became very viscous and an amorphous solid

on cooling. This did not occur because of a chemical reaction but was probably due to the formation of a gel. The material was dissolved in ether, washed with sodium bicarbonate solution and dried. This operation allowed recovery of the starting alcohol which was then successfully dehydrated with sulfuric acid.

When p-toluenesulfonic acid was used as the dehydrating agent, the reaction proceeded very slowly and was successful only for the compounds with a methyl or ethyl substituent at the two position. Of all the methods used, this seemed to be the most useful. There appeared to be little or no rearrangement occurring, and only very small amounts of tarry biproducts were formed. In those cases where the dehydration was successful, the yields were good. Possibly a better method would be reaction with thionyl chloride followed by dehydrohalogenation with pyridine. This method might work on the compounds which cannot be dehydrated with acid.

In the lithium bromide dehydration of those compounds with a t-butyl group in the 4-position, elemental analysis indicated the possible formation of 2,6,6-trimethyl-1-alkylcyclohept-3-enol (Figure 15). Precedence for this reaction is found in the dealkylation of 1,3,5-tri-t-butylbenzene to m-di-t-butylbenzene and t-butylbenzene in benzene with sulfuric acid as the catalyst (Figure 15).

In the synthesis of 2,6,6-trimethyl-3-t-butylcyclohept-4-enone, a solid material was obtained in the pot residue from the final distillation. The molecular weight and elemental analysis indicated that the material was a dimeric ketone. The infrared spectrum (Figure 17) corresponded to the isomeric dieucarvelones reported by Buchi and Saari[41] and others[42,43]. A possible mechanism for this synthesis is given in Figure 8.

The bromination/dehydrobromination steps were not as successful as expected. The N-bromosuccinimide reacted quantitatively as indicated by the recovered succinimide. However, on dehydrobromination it was found that the major portion of the product was recovered diene. Only minor amounts of the desired trienes were obtained. It appears possible that some of the bromine may have added to a double bond of the dienes instead of, or, in addition to allylic substitution. A dark, high-boiling liquid was obtained in addition to the hydrocarbons in the dehydrobrominations. This material could possibly have been a bromide. The conditions used for dehydrobrominations would not have completely removed the bromine from such a compound.

In the attempted synthesis of the 2,3,5,7,7-pentasubstituted tropilidenes, the 5-triphenylmethyl carenone was not obtained. It was found that the enol ether could be formed by modifying the conditions originally used by Conrow. The dioxane solution of the crude reaction mixture was evaporated to about one-half its original volume instead of to dryness. At this point an immiscible oil separated which was dissolved in ethanol and cooled several days in a refrigerator. The crystalline material which formed gave an infrared spectrum (Figure 18) consistent with an enol ether. The substance was recrystallized from Skelly B in an attempt at purification. A material resulted whose infrared spectrum (Figure 19) and melting point were identical with those for the bicyclic ketone reported by Conrow and Doering. Attempts to recrystallize from ethanol, the solvent used by Conrow and Doering, resulted in trapping the triphenylmethyl ion by the ethanol to give triphenylmethyl ethyl ether and eucarvone. All attempts at purification resulted in loss of the compound. It seems probable that both Conrow and Doering obtained the enol ether, but due to its great instability it rearranged under the more extreme conditions of work-up.

Recently Knox, Velarde and Cross[48] reported the stable enol ether XXIX (Figure 4). The compound appeared to be stanilized by the 1,6-bridge. NMR spectra showed that the compound was monocyclic. This data led to the proposal that the eucarvone enol triphenylmethyl ether was also monocyclic. The structure and mechanism for the synthesis are given in Figure 9.

The syntheses of the 2,3,6,7,7-pentasubstituted tropilidenes proceeded through the initial stages quite well. The formation of the nitrilium perchlorate salt occurred in lower than literature yields[46], but usable amounts were obtained. The low yield is probably due the steric hindrance of the 2-alkyl group on the acetonitrile at the one position. This is evidenced by the fact that lower yields were obtained when an ethyl group was in the 2 position than when a methyl group was there. A slight excess of lithium hydride with a catalytic amount of sodium borohydride was chosen as the reducing agent in an attempt to prevent reduction of the conuugated diene in addition to the carbon-nitrogen triple bond. It was hoped that any diborane formed from the sodium borohydride would be reconverted to the borohydride by the lithium hydride. Quantitative yields were obtained for the reduction to the amine.

It was expected that in the final elimination step, the cyclic triene would be formed as the most stable olefinic product. Competing reactions were expected to be the removal of the beta-hydrogen in the ethyl group to form ethylene, and reaction with solvent to form an alcohol (Figure 14). If ethylene were formed, the tertiary amine could be remethylated, and the reaction repeated. There was no evidence of this occurring. There was some difficulty in finding a solvent for the quaternary ammonium iodide, and the best one available appeared to be a mixture of methanol and water. Therefore, there appeared to be no way of preventing reaction with solvent.

The conjugated olefin should be very subject to oxidation, and silver salts in basic solution have considerable oxidizing power. This could possibly be avoided by use of a different base. Thallous oxide would be one possibility, and since the quaternary ammonium oidide should be fairly reactive, excess potassium hydroxide should be a suitable base.

It is assumed that either oxidation or polymerization was the cause for the failure of the Hofmann elimination.

Although the goal of the synthesis and identification of a series of highly substituted tropilidenes was not attained, the exploratory experiments reported here do serve to make some interesting points. They form a basis for future work in this general area. Particular suggestions for improving the synthetic schemes have been made in the course of the preceding disucssion. General areas which should prove interesting for further study are the transannular ether formation which was apparently intervening in the dehydration of 2,6,6-trimethyl-1,3-diisopropylcyclohept-4-enol, 2,6,6-trimethyl-1-t-butyl-3-isopropylcyclohept-4-enol, and 2,6,6-trimethyl-1-isopropyl-3-t-butylcyclohept-4-enol, the apparent failure in the allylic bromination steps, and the apparent formation of the genuine enol ether as a precursor to or simultaneous with the formation of the 5-triphenylmethyl carenone.

EXPERIMENTAL PROCEDURES

GENERAL: Infrared spectra were taken on Perkin Elmer Model 137 and Infracord Spectrophotometers. Solids were run as potassium bromide pellets and liquids as films on salt plates. Ultraviolet spectral data were obtained with a Beckman DB Spectrophotometer. Melting points were obtained using either

sealed capillary tubes in a circulating oil bath or a Fisher-Johns Melting
Point Apparatus. All melting points and boiling points are uncorrected.
Analyses were run by Galbraith Laboratories, Inc., Knoxville, Tennessee.

EUCARVONE: The procedure used was that of Corey and Burke[15]. 1-Carvone
(191 g., 0.665 moles) was added to a solution of 150 g. (1.84 moles) of
hydrobromic acid (500 g. of a solution of hydrogen bromide, 30-32% in acetic
acid). The reaction flask was cooled to -36.5° C. (ethylene dichloride-dry
ice). Addition required about thirty minutes.

The resulting dark solution was poured into one liter of water, and the
lower, dark layer was separated and washed with sodium bicarbonate solution
and water until neutral. The aqueous layer and washings were extracted with
ether, and the organic layers were combined and dried over anhydrous mag-
nesium sulfate.

.The dried solution was dropped into a well-cooled (ice-salt) and well-
stirred solution of 72.5 g. (1.3 moles) of potassium hydroxide in 275 ml. of
methanol. After addition was completed, the resulting suspension was heated
under reflux with stirring for 15 minutes at about 50° C. It was then cooled
to room temperature and poured onto an ice-sulfuric acid mixture (about 175
ml. of concentrated acid) to precipitate the eucarvone. The yellow oil
separated, the aqueous layer was extracted with ether, and both organic
layers were washed with sodium bicarbonate solution and water.

The crude eucarvone was steam distilled, and the product was
fractionally distilled at 80-93° C. (7-9 mm.). VPC with a 30% cyanosilicone
column showed essentially one peak, and the IR spectrum agreed with the lit-
erature for eucarvone. The yield for the preparation was 39-53% for four
attempts.

2,6,6-TRIMETHYL-3-tert-BUTYLCYCLOHEPT-4-ENONE: The procedure used was from
K. Conrow[40]. Short lengths of magnesium ribbon (27.9 g., 1.15 moles) were
placed in a 1000 ml. three-necked flask with a crystal of iodine and 100 ml.
of absolute ether. The flask was fitted with a relux condenser, electric
stirrer, dropping funnel and calcium chloride tubes. t-Butyl chloride
(134.3 g., 1.45 moles) in 150 ml. of absolute ether was added dropwise
with ice-cooling. The reaction stood at room temperature for about one-
half hour and was heated under reflux for one-half hour.

Eucarvone (82.6 g., 551 moles) in 100 ml. absolute ether was added
dropwise with cooling and stirring. The reaction mixture was stirred over-
night at room temperature.

A solution of 75 g. of ammonium chloride in 300 ml. of water was
added to the reaction mixture with cooling and stirring. The ether layer
was separated, and the aqueous layer was extracted with ether. The organic
layers were combined and dried over magnesium sulfate.

The dried solution was concentrated and fractionally distilled. The
ketone product was collected at 80-87° C. (1 mm.). VPC showed essentially
one peak. The IR spectrum showed the expected carbonyl peak (1700 cm^{-1})
and the presence of the t-butyl group was indicated (1195, 1290, 1350, 1450,
2800 cm^{-1}). The yield for the reaction was 67.8 g. (59.7%).

After standing for several days, a white precipitate formed in the pot
residue. The crystals were collected and recrystallized from acetonitrile
three times. The yield was 1.82 g. The crystals were found to sublime, and
this property was used for a final purification step.

Anal. Calcd. for $C_{20}H_{30}O_2$: C, 79.4; H, 9.93. Found: C, 78.91;
H, 9.97.

This information corresponds with the dimer reported by Buchi and Saari[41] and others[42,43]. The IR spectrum fits that reported by these authors, and the melting point (163-172° C.) agrees generally with a mixture of the isomers that were reported.

2,3,7,7-TETRAMETHYL-4-tert-BUTYL-1,3,5-CYCLOHEPTATRIENE: Methyl magnesium iodide was prepared from 7.92 g. (330 mmoles) of magnesium ribbon and 53.6 g. (377.5 mmoles) of methyl iodide. The magnesium in about 100 ml. of anhydrous ether was placed in a one liter flask with a crystal of iodine. The methyl iodide in about 140 ml. of ether was added dropwise with cooling after the reaction had been initiated. After addition was complete the mixture was stirred at room temperature for one-half hour and then was heated under reflux for one-half hour.

2,6,6-Trimethyl-3-tert-butylcyclohept-4-enone (34.0 g., 163.5 mmoles) in 140 ml. of ether was dropped into the reaction mixture with cooling and stirring. After addition, the mixture was stirred at room temperature for one-half hour and then was heated under reflux for about one hour. The mixture then stood overnight.

A solution of 62.5 g. of ammonium chloride in 250 ml. of water was dropped into the reaction mixture with cooling and stirring. The ether layer was separated, and the aqueous layer was extracted with ether. The combined organic layers were washed with sodium bicarbonate solution and water and dried over magnesium sulfate.

The ether was distilled from the dried solution. The IR spectrum showed the presence of a small amount of ketone (carbonyl peak at about 6 μ) along with the expected alcohol.

The intermediate alcohol was dehydrated with sulfuric acid. The alcohol was placed in a 100 ml. flask connected to a distilling apparatus, and three drops of concentrated sulfuric acid were added. The mixture was heated at 70-80° C. (20 mm.). A small amount of water was removed by distillation. The pot mixture was dissolved in ether, washed with sodium bicarbonate solution and water, and dried over magnesium sulfate. The ether solution was concentrated, and an IR was run which indicated that the dehydration was not complete. The dehydration was continued with 12 g. of boric acid. The remaining water distilled from the mixture at 80-85° C. (3-40 mm.). The dehydration product was worked up as before. The IR spectrum showed no significant -OH peak. The crude dehydration product was fractionally distilled at 70° C. (1.4 mm.) -90° C. (1.8 mm.) giving 20 g. of product. The yield for the sequence through dehydration was 59%.

.The dehydration product, assumed to be 2,3,7,7-tetramethyl-4-tert-butyl-1,5-cycloheptadiene, was allylically brominated[44]. The diene (20 g.) was dissolved in 115 ml. of carbon tetrachloride. An equimolar amount of N-bromosuccinimide (17.3 g.) was added and the mixture was boiled under reflux for eleven hours. The end of the reaction was indicated by insoluble succinimide which floated to the surface and by a negative starch-iodide test.

The solid succinimide was removed by filtration, and 40 ml. of ethanolic potassium hydroxide (15.9 g. of potassium hydroxide in 100 ml. of ethanol) were added to effect dehydrohalogenation. The mixture was heated under reflux for about 30 minutes. The crude product was washed with boric acid solution and water, and the washings were extracted with carbon tetrachloride. The combined organic layers were dried over magnesium sulfate.

The dried product was concentrated and fractionally distilled. The product was collected at 64-67° C. (1.5 mm). VPC showed the presence of one large and two small peaks. The large peak was the only one separated with practicality by gas chromatography. The IR was the same as for the diene. The compound showed no UV absorption in the region expected for trienes. Analysis confirmed the fact that this compound was recovered diene. The triene was obtained in only trace amounts.

Anal. calcd. for $C_{15}H_{26}$: C, 87.38; H, 12.62. Found: C, 87.11; H, 13.00.

3,7,7-TRIMETHYL-2-ETHYL-4-tert-BUTYL-1,3,5-CYCLOHEPTATRIENE: The procedure was generally the same as for the preceding compound of the series. The ethyl Grignard reagent was prepared from 6.0 g. (244 mmoles) of magnesium ribbon (short lengths) and 28.5 g. (260 mmoles) of ethyl bromide. The magnesium was placed in a flask with 25 ml. of anhydrous ether and an iodine crystal. The ethyl bromide in 75 ml. of anhydrous ether was dropped into the mixture with cooling and stirring. After addition, the mixture stood at room temperature for 30 minutes and was heated under reflux for 30 minutes.

2,6,6-Trimethyl-3-tert-butylcyclohept-4-enone (33.8 g., 163 mmoles) was added to the reaction mixture dropwise with cooling and stirring. The mixture then stood at room temperature for 20 minutes, was heated under reflux for 30 minutes, and stood overnight.

A solution of 50 g. of ammonium chloride in 200 ml. of water was dropped into the reaction mixture with ice-salt cooling and stirring. The ether layer was separated, and the aqueous layer was extracted with ether. The combined organic layers were dried over magnesium sulfate. The ether

was removed by distillation. An IR spectrum of the crude alcohol showed a strong -OH peak at 3 and a small amount of unreacted ketone (carbonyl peak at about 6μ).

Dehydration of the alcohol was attempted by distilling from 5 g. of lithium bromide at 140° C. (30 mm.). Some dehydration occurred as was shown by a small amount of water which was distilled from the mixture. Foaming was excessive, however, so the lithium bromide was removed by washing with water and redrying the alcohol with magnesium sulfate. An IR spectrum was run and appeared essentially unchanged. Three drops of concentrated sulfuric acid were added, and the dehydration was run at 100° C. (20-25 mm.). The crude dehydration product was washed with sodium bicarbonate solution and water and dried over magnesium sulfate. The product was fractionally distilled at 70° C. (1.5 mm.) -90° C. (2.0 mm.). The yield was 23.4 g. (65.5%). The IR spectrum showed no -OH peak.

The product, presumably 3,7,7-trimethyl-2-ethyl-4-tert-butyl-1,5-cycloheptadiene (23.4 g., 106 mmoles) was subjected to allylic bromination by heating under reflux with an equimolar amount (19.0 g.) of N-bromosuccinimide for 11.5 hours. The end of the reaction was determined as before by a negative starch-iodide test and the presence of succinimide floating in the reaction mixture.

The solid succinimide was removed by filtration, and the solution remaining was heated under reflux with 40 ml. of ethanol potassium hydroxide for about 30 minutes. The crude product was washed with boric acid and water and dried over magnesium sulfate.

The carbon tetrachloride was removed by distillation, and the crude product was fractionally distilled. Six fractions were collected totaling

13.64 g. VPC of these six cuts showed three major hydrocarbon peaks plus several materials of much higher retention times. The first two fractions collected contained a much greater percentage of these three hydrocarbons. IR spectra indicated that the last four fractions contained large quantities of carbonyl compounds and halides while the first two fractions appeared to have only C-H, C-C, and C-C absorption.

The two hydrocarbon fractions were combined and redistilled using a spinning band column. Cut one, 100° C. (10 mm.) -102° C. (10.5 mm.), contained the first two of the VPC peaks. Cut two, 100° C. (10 mm.) -104° C. (11 mm.), and cut three, 105° C. (10.5 mm.) -108° C. (11 mm.), both contained all three of the VPC hydrocarbon peaks. Cut Four, collected very slowly at 102° C. (10 mm.), was essentially the pure third VPC peak.

Cut 4 contained the majority of the material obtained from the last step in the synthesis. This material gave an IR spectrum identical with the starting diene. The material did not absorb in the UV region expected for the diene. Analysis indicated the material was actually the diene. The triene if formed was in the first three distillation cuts in small amounts.

Anal. Calcd. for $C_{16}H_{28}$: C, 87.27; H, 12.73. Found: C, 87.05; H, 13.08.

ATTEMPTED PREPARATION OF 3,7,7-TRIMETHYL-2-ISOPROPYL-4-tert-BUTYL-1,3,5-CYCLOHEPTATRIENE: Isopropyl Grignard reagent was prepared from 8.62 g. (359 mmoles) of magnesium ribbon strips and 50.5 g. (410 mmoles) of isopropyl bromide using the previously described procedure. 2,6,6-trimethyl-3-tert-butylcyclohept-4-enone (37.2 g., 178 mmoles) in 110 ml. of ether was dropped into the reaction mixture with cooling and stirring. The resulting mixture was subjected to the same work-up as described for the previous Grignard reactions. The IR spectrum of the product showed a strong -OH

peak and a small carbonyl peak indicating the presence of a small amount of unreacted starting ketone.

An attempt was made to dehydrate the crude alcohol by heating it with 10 g. of anhydrous lithium bromide at 100° C. (2-10 mm.). As the water was removed, it was distilled from the mixture and collected. The process was run for about 10 hours. The product was taken up in ether, washed with water to remove the lithium bromide, and dried over magnesium sulfate.

Fractional distillation gave eleven cuts. IR spectra were run on these fractions. Fraction one appeared from its spectrum to be hydrocarbon in nature since no other functional group absorption appeared. Fractions 2-7 contained large amounts of unreacted ketone as judged by the absorption in the carbonyl region of the spectrum. Fractions 8-11 appeared to be mostly undehydrated alcohol as indicated by the absorption at about 3500 cm^{-1}.

·The distillation fraction one was found to contain sixteen major peaks. The other distillation fractions had similarly large numbers of VPC peaks. These peaks were so close together as to be virtually impossible to separate.

As the last fraction was collected in the preceding distillation, a solid material began to sublime from the pot. A total of 4.76 g. of this white crystalline solid was collected. The material was purified by re-crystallization from acetonitrile and by sublimation. The melting point was $73.5-74.5^\circ$ C. The IR spectrum indicated that it was an alcohol. The evidence points to the dealkylation of the alcohol with loss of the t-butyl group.

Anal. Calcd. for $C_{13}H_{24}O$: C, 79.59; H, 12.29. Found: C, 79.07; H, 12.15.

The preceding synthesis was repeated giving 60 g. of the alcohol. To the alcohol was added 20 ml. of glacial acetic acid and then 10 ml. of

concentrated sulfuric acid. The mixture was heated at 100° C. for about one hour. It was then poured over about 500 g. of ice. The organic material was taken up in ether and washed with sodium bicarbonate solution and water. The ether was removed by distillation, and the product was fractionally distilled. The distillation gave: cut one, 62° C. (2.5 mm.) -80°C. (1.9 mm.); cut two, 74° C. (2.0 mm.) -75° C. (1.9 mm.); cut three, 80° C. (2.2 mm.) -82° C. (1.9 mm.); and a large amount of black, tarry residue. IR spectra were run for the three cuts. Cuts one and two showed no -OH absorption, but there was strong absorption at 1175 cm^{-1} which is consistent with an ether. Cut three appeared from its IR spectrum to be a hydrocarbon. This probably was a mixture of isomers of the desired product. It was not considered profitable to attempt a VPC separation of the materials in these cuts.

3,7,-TRIMETHYL-2,4-DI-tert-BUTYL-1,3,5-CYCLOHEPTATRIENE: Using the procedure described previously, t-butyl Grignard reagent was prepared from 9.55 g. (397 mmoles) of magnesium ribbon strips and 44 g. (475 mmoles) of t-butyl chloride. 2,6,6-Trimethyl-3-t-butylcyclohept-4-enone (37 g., 178 mmoles) in 100 ml. of anhydrous ether was dropped into the reaction mixture with cooling and stirring. The work-up was the same as for the preceding Grignard reactions. The IR spectrum showed a strong -OH peak at about 3600 cm^{-1} and a small carbonyl peak at about 1710 cm^{-1}. This indicated the presence of a small amount of unreacted ketone with the alcohol. The yield was 42.7 g. (90%).

Dehydration of the crude alcohol was attempted using 13 g. of boric acid as the dehydrating agent. About 2 g. of water was collected by distilling at 60° C. (50-60 mm.). After 9-10 hours the alcohol began to get

very viscous and an amorphous solid formed on cooling. This material was dissolved in ether and washed with sodium bicarbonate solution and water to remove the boric acid. The ether layer was dried over magnesium sulfate, and the ether was removed by distillation. An IR spectrum indicated incomplete dehydration by the presence of -OH absorption at about 3600 cm^{-1}. Sulfuric acid (5-6 drops) was added to the alcohol and distillation was resumed. Dehydration proceeded slowly over a period of six days. The process was carried out at 50° C. (2.5 mm.) -85°C. (0.6 mm.). The product was dissolved in ether and washed with sodium bicarbonate solution and water. The ether solution was dried over magnesium sulfate, and the ether was removed by distillation. Fractional distillation at 50° C. (1.0 mm.) -59° C. (1.4 mm.) gave 16.0 g. of product (40% yield). VPC with an SF-96 column showed three peaks. The IR spectrum indicated the product was an unsaturated hydrocarbon: λ_{max}. 2985-2995 cm^{-1}, 750 cm^{-1}, and 1350-1475 cm^{-1} (C-H); 1630 cm^{-1} and 1680 cm^{-1} (C=C).

The preceding product (15.2 g., 61.3 mmoles) was dissolved in 250 ml. of carbon tetrachloride and subjected to allylic bromination by heating under reflux for ten hours with an equimolar amount of N-bromosuccinimide (10.9 g.). The end of the reaction was indicated by a negative starch-iodide test.

The solid succinimide was removed by filtration. About one-half of the carbon tetrachloride was removed by distillation. During the distillation the brominated hydrocarbons began to spontaneously lose hydrogen gromide gas. 2,4,6-Trimethylpyridine (13 g., 107 mmoles) was added to the mixture to effect dehydrohalogenation. The mixture of base and bromide was heated under reflux for 3.5 hours, and the solid pyridinium salt was removed

by filtration. The carbon tetrachloride solution was washed with boric acid solution and water to remove any remaining base and salt.

The carbon tetrachloride was removed by distillation, and the crude product was fractionally distilled giving 6.79 g. of product at 50° C. (1.2 mm.) -62° C. (1.0 mm.). The yield for the final step was 10% and the overall yield for the sequence was 3%.

VPC showed only two peaks. These peaks were easily separated by VPC. Peak one was found to be the triene, and peak two was recovered diene. The IR spectrum was consistent with that expected for the triene.

Anal. Calcd. for $C_{18}H_{30}$: C, 87.80; H, 12.20. Found: C, 87.99; H, 12.11.

2,6,6-TRIMETHYL-3-ISOPROPYLCYCLOHEPT-4-ENONE: The procedure followed in this synthesis was the same as that previously described for its 3-t-butyl analog. The isopropyl Grignard reagent was prepared from 50.8 g. (2.08 moles) of magnesium ribbon strips and 325.2 g. (2.64 moles) of isopropyl bromide. This Grignard reagent was then reacted with 150.8 g. (1.00 mole) of eucarvone. Work-up as usual resulted in a crude product whose IR spectrum was the same as a sample which had been purified by VPC. The ketone was fractionally distilled at 75° C. (0.7 mm.) -76° C. (0.4 mm.). The yield was 134 g. (69%).

2,3,7,7-TETRAMETHYL-4-ISOPROPYL-1,3,5-CYCLOHEPTATRIENE: The methyl Grignard reagent was prepared from 7.82 g. (322 mmoles) of magnesium ribbon strips and 52.3 g. (368 mmoles) of methyl iodide. The Grignard reagent was reacted with 31 g. (160 mmoles) of 2,6,6-trimethyl-3-isopropylcyclohept-4-enone, and the product was worked up by the method previously described.

The ether was distilled from the crude alcohol. Dry, thiophene-free benzene (50 ml.) and a bit of p-toluenesulfonic acid were added to the

alcohol in a 100 ml. round-bottomed flask. The flask was connected to a Dean-Stark trap fitted with a reflux condenser. The mixture was then boiled under reflux for 42 hours to achieve dehydration. The yield of water collected was 2.9 g. (90%). The crude product was washed with sodium bicarbonate solution and water and dried over magnesium sulfate. The benzene was removed by distillation, and the product was fractionally distilled. The product was collected at 62-65° C. (2.0-2.2 mm.). The yield was 27.0 g. (88%). The IR spectrum showed no -OH peak and no carbonyl peak and was consistent with the expected diene: $\lambda_{max.}$ 2850-2930 cm^{-1}, 1370-1460 cm^{-1}, 735 cm^{-1}, 840 cm^{-1}, 870 cm^{-1}(C-H); 1630 cm^{-1} and 1690 cm^{-1} (C=C).

The product, assumed to be 2,3,7,7-tetramethyl-4-isopropyl-1,5-cycloheptadiene, was subjected to allylic bromination. The olefin (24.0 g., 125.5 mmoles) was dissolved in 400 ml. of carbon tetrachloride in a 1000 ml. flask. The N-bromosuccinimide (22.3 g., 125.5 mmoles) was added, and the mixture was heated under reflux with stirring for about eight hours. The end point was indicated by a negative starch-iodide test.

The solid succinimide was removed by filtration, and the solution was concentrated to about one-half of its original volume. The brominated product began to dehydrobrominate spontaneously during the concentration. 2,4,6-Trimethylpyridine (25 g., 206 mmoles) was added. The base began to react immediately forming a dark precipitate. The mixture was heated under reflux for 3.5 hours. The pyridinium salt was removed by filtration, and the solution remaining was washed with boric acid solution and water to remove any base or salt remaining. The solution was dried and fractionally distilled. A product was collected at 48° C. (1.2 mm.) -67° C. (1.9 mm.). The yield for the final step was 6.50 g. This material contained three components as indicated by VPC. Only small amounts were found to be triene

with the majority being recovered diene. No practical method for separating the triene from the other material was found. Only the diene was recovered pure.

Anal. Calcd. for $C_{14}H_{24}$: C, 87.50; H, 12.50. Found: C, 87.65; H, 12.35.

3,7,7-TRIMETHYL-2-ETHYL-4-ISOPROPYL-1,3,5-CYCLOHEPTATRIENE: The ethyl Grignard reagent was prepared from 7.82 g. (322 mmoles) of magnesium ribbon strips and 40.1 g. (368 mmoles) of ethyl bromide. It was then reacted with 31 g. (160 mmoles) of 2,6,6-trimethyl-3-isopropylcyclohept-4-enone. The IR spectrum after work-up showed no significant carbonyl absorption and showed -OH peak at about 3600 cm^{-1}.

The crude alcohol was placed in a 100 ml. round-bottomed flask with 60 ml. of dry, thiophene-free benzene and a bit of p-toluenesulfonic acid. The flask was connected to a Dean-Stark trap fitted with a reflux condenser. The mixture was then boiled vigorously under reflux for about 144 hours. From the amount of water produced (2.9 g.), the reaction appeared quantitative. The IR spectrum after work-up showed no -OH peak. The product was fractionally distilled at 69° C. (2.0 mm.) -74° C. (2.9 mm.) yielding 25.7 g. (78%) of a material assumed to be the diene. The IR spectrum of the product was consistent with the expected olefin: $\lambda_{max.}$ 1695 cm^{-1} and 1645 cm^{-1} (C=C); 2850-2950 cm^{-1}, and 740 cm^{-1} (C-H). VPC showed three major peaks.

The olefin, assumed to be 3,7,7-trimethyl-2-ethyl-4-t-butyl-1,5-cycloheptadiene and isomers, was subjected to allylic bromination. The olefin, dissolved in 400 ml. of carbon tetrachloride, was boiled under reflux for 7.5 hours with an equimolar amount of N-bromosuccinimide. The end-point was recognized by a negative starch-iodide test. The solid

succinimide was removed by filtration, and the remaining solution was concentrated to remove the carbon tetrachloride. The product was dehydrobrominated by heating for four hours at 85-90° C. with 17.0 g. (0.14 moles) of 2,4,6-trimethylpyridine. The mixture was filtered to remove the solid salt, and the liquid was heated to 90° C. for three hours longer. The solid salt was again removed by filtration, and the product was fractionally distilled after work-up. The fraction collected at 57° C. (1.2 mm.) -64° C. (1.3 mm.) gave 5.0 g. of product. VPC showed the presence of three peaks. The major fraction and the only one obtained pure was the starting material diene.

Anal. Calcd. for $C_{15}H_{26}$: C, 87.38; H, 12.62. Found: C, 87.51; H, 12.39.

ATTEMPTED SYNTHESIS OF 3,7,7-TRIMETHYL-2,4-DIISOPROPYL-1,3,5-CYCLOHEPTA-TRIENE: The isopropyl Grignard reagent was prepared from 7.82 g. (322 mmoles) of magnesium ribbon strips and 45.3 g. (368 mmoles) of isopropyl bromide. The reagent was reacted with 33.0 g. (170 mmoles) of 2,6,6-trimethyl-3-isopropylcyclohept-4-enone. After work-up, the IR spectrum showed evidence of a significant amount of unreacted ketone along with the expected alcohol.

The alcohol was subjected to dehydration conditions by dissolving it in 50 ml. of benzene with a bit of p-toluenesulfonic acid and boiling vigorously under reflux. After 48 hours no dehydration was observed, so more p-toluenesulfonic acid was added and the boiling continued. About 24 hours later no dehydration was observed. In order to raise the temperature of the boiling mixture, 40 ml. of xylene were added and the boiling was continued. After 13 days, the procedure was stopped, and the mixture was

washed with sodium bicarbonate solution and water. It was dried over magnesium sulfate. The IR was still the same as the previous IR for the alcohol.

The benzene and xylene were removed from the alcohol by distillation. It was then placed in a 100 ml. flask and to it was added 15 ml. of glacial acetic acid and 7.5 ml. of concentrated sulfuric acid respectively. The mixture was boiled at 120° C. (bath temperature) for 1.5 hours and poured onto 400 ml. of ice. The organic layer was dissolved in ether, and the aqueous layer was extracted with ether. The organic layers were washed with sodium bicarbonate solution and water and dried over magnesium sulfate. The product was fractionally distilled giving a product at 57-62° C. (0.8 mm.). Only a very small amount was obtained. The remainder of the organic material was a black tar. The IR spectrum indicated the possible presence of an ether. There was no -OH absorption, but there is a large peak at 1120 cm^{-1}. The material does not appear to be saturated.

ATTEMPTED SYNTHESIS OF 3,7,7-TRIMETHYL-2-tert-BUTYL-4-ISOPROPYL-1,3,5-CYCLOHEPTATRIENE: The t-butyl Grignard reagent was prepared from 8.31 g. (342 mmoles) of magnesium ribbon strips and 37.1 g. (401 mmoles) of t-butyl chloride. The reagent was reacted with 31.5 g. (162 mmoles) of 2,6,6-trimethyl-3-isopropylcyclohept-4-enone. After the usual work-up, the IR spectrum showed a small amount of unreacted ketone and the expected strong -OH absorption at about 3600 cm^{-1}.

The crude alcohol was subjected to dehydration conditions by adding 50 ml. of xylene and a bit of p-toluenesulfonic acid and boiling under reflux. The reaction flask was attached to a Dean-Stark trap and a reflux condenser. The mixture did not boil very vigorously at 140-150° C. (bath temperature), and rather than raise the temperature higher, 40 ml. of benzene were added.

The boiling was continued vigorously at the same bath temperature. After two weeks of this procedure, no dehydration was observed. The mixture was washed with sodium bicarbonate solution and water and dried. An IR spectrum of the dried material was the same as the starting material.

The benzene and xylene were removed by distillation. The alcohol was then reacted with glacial acetic acid (15 ml.) and concentrated sulfuric acid (7.5 ml.) in the manner previously described and worked-up. Fractional distillation gave a product at 60-62° C. (0.8 mm.) which appeared to be an ether. There was no -OH or double bond absorption in the IR spectrum, and there was a very large peak at 1130 cm^{-1}. VPC showed four peaks of equal size and practically on top of each other. This is consistent with the expected four possible isomers for the transannular ether.

Anal. Calcd. for $C_{17}H_{32}O$: C, 80.95; H, 11.91. Found: C, 81.94; H, 12.21.

A few drops of an unsaturated material was obtained which had no -OH absorption. VPC showed many peaks indicating the probability of extensive rearrangement accompanying any dehydration. Most of the starting material was converted to tars.

2,3,7,7-TETRAMETHYL-1,3,5-CYCLOHEPTATRIENE: The methyl Grignard reagent was prepared from 10 g. (417 mmoles) of magnesium ribbon strips and 70 g. (493 mmoles) of methyl iodide. It was reacted with 50 g. (333 mmoles) of eucarvone. After the usual work-up, an IR spectrum was run which showed a small carbonyl absorption and no -OH peak. The spectrum was consistent with the dehydration product of the expected alcohol. It was assumed that spontaneous dehydration occurred sometime during the work-up. The crude product was fractionally distilled at 50° C. (4.5 mm.) -65° C. (10 mm.). The yield was 28.6 g. (58%). VPC with a dioctyl phthalate column showed two peaks

which were assumed to be the desired triene and its isomer with the third double bond exocyclic to the ring[31]. λ_{max}: 1600 cm^{-1}, 1630 cm^{-1}, and 1670 cm^{-1} (C=C); 2900-3000 cm^{-1}, 1440-1480 cm^{-1}, 1360 cm^{-1}, 1390 cm^{-1}, 845 cm^{-1}, 775 cm^{-1}, and 725 cm^{-1} (C-H).

ATTEMPTED SYNTHESIS OF 2,3,7,7-TETRAMETHYL-6-TRIPHENYLMETHYL-1,3,5-CYCLO-HEPTATRIENE: Using the procedure of Hofmann and Kirmreuther[45], triphenyl-methyl perchlorate was prepared. Triphenylcarbinol (35 g., 134 mmoles) was suspended in 130 ml. of acetic anhydride. Perchloric acid (34 ml. of 70% acid) was added to the suspension dropwise with ice-cooling and stir-ring. An orange-red precipitate formed immediately and was removed by filtering with a sintered glass funnel. The precipitate was washed with acetic anhydride and ether and dried in air. The yield was 42.2 g. (91%).

Using the procedure of Conrow[46], N-(5-triphenylmethyl-1,2,6,6-tetramethylcyclohepta-1,3-dien-6-yl)-acetonitrilium perchlorate was pre-pared. To a suspension of 1.0 g. (2.9 mmoles) of freshly prepared trityl perchlorate in 8.7 ml. of dry acetonitrile was added 0.5 ml. (about 3 mmoles) of 2,3,7,7-tetramethylcycloheptatriene. A darker red color formed immediately, and the trityl perchlorate gradually dissolved. The solution lightened slightly and white crystals began to form. These crystals were collected after 1.3 hours. A second crop of crystals was obtained by evaporation of the liquid, addition of ethyl acetate, evaporation, a second addition of ethyl acetate with trituration, and filtration. The combined weight of products was 0.3 g. (19.5% yield). The process was repeated to give a total of 18 g. of the nitrilium salt. The IR spectrum of the salt gave λ_{max}: 2900 cm^{-1}, 1450 cm^{-1}(-CH$_3$); 1650 cm^{-1}(C=C); 770 cm^{-1}(C-H); 1110 cm^{-1}(perchlorate); 1600 cm^{-1}, 750 cm^{-1}, 710 cm^{-1}(C-H). The crystals melted at 205.5-206.5° C.

Reduction of the carbon-nitrogen triple bond was accomplished using a sodium hydride-sodium borohydride mixture. The sodium hydride (2.17 g., 90 mmoles) was suspended in glyme which had been freshly distilled from lithium aluminum hydride. A catalytic amount of sodium borohydride was added. The nitrilium salt was suspended in glyme and dropped into the hydride solution. The mixture was heated under reflux for 2.5 hours. After cooling to room temperature, water was added to hydrolyze the excess sodium hydride, and dilute hydrochloric acid was added to hydrolyze the sodium borohydride. The solvent was evaporated to about one-half volume, and 6.0 g. of crystalline product were collected. The crystals melted at 142-144° C. The IR spectrum showed the loss of the strong peak at 1110 cm^{-1} and the presence of a peak at 3500 cm^{-1} for the amine. A solution of the crystals was strongly basic. To obtain the free base, the crystals were dissolved in glyme and washed with aqueous sodium hydroxide.

Anal. Calcd. for $C_{32}H_{38}NCl$: C, 81.44; H, 8.06; N, 2.97. Anal. Calcd. for $C_{32}H_{37}N$: C, 86.43; H, 8.50; N, 3.22. Found: C, 84.63; H, 8.38; N, 3.47.

Analysis indicates that the material obtained was probably a mixture of the salt of the amine and the free amine.

The amine (18.5 g., 45 mmoles) was dissolved in a 1:1 mixture of acetone and Skelly B. Methyl iodide (25 g., 176 mmoles) was added, and the mixture was stirred for three hours at room temperature. Light colored crystals began to form, and the mother liquor turned a dark rust color. Stirring continued overnight. After 16 hours the ctystals were collected (3.4 g.). The liquid was stirred about two hours longer, and more crystals (1.3 g.) were collected. The total yield was 18%. The product showed the presence of halogen when tested with silver nitrate solution.

The product, probably the quaternary ammonium iodide (2.5 g., 4.2 mmoles), was dissolved in 80 ml. of methanol and 50 ml. of water. Silver oxide (2.0 g., 8.5 mmoles) was added, and the mixture was stirred overnight (about 22 hours) at room temperature. The reaction mixture was rapidly filtered with suction. The solid collected was washed with water, and the wash was added to the mother liquor causing the formation of a cloudy suspension. The solvent was removed under vacuum. The solid residue was heated at 80-90° C. (15 mm.) for about 45 minutes. The solid melted and there was evidence of gas evolution. The product was dissolved in ether. The dissolved material was washed with dilute hydrochloric acid to remove any amines. The ether was evaporated leaving a gummy solid material. The IR spectrum of this material showed no evidence that it was the desired product.

3,7,7-TRIMETHYL-2-ETHYL-1,3,5-CYCLOHEPTATRIENE: The ethyl Grignard reagent was prepared from 12.4 g. (499 mmoles) of magnesium ribbon strips and 58.6 g. (532 mmoles) of ethyl bromide. The Grignard reagent was reacted with 50.2 g. (333 mmoles) of eucarvone. After the usual work-up procedure, an IR spectrum was taken which showed strong evidence of the presence of an alcohol (absorption at 3450 cm^{-1}), and evidence of some unreacted ketone or a new ketone formed by 1,4-addition (absorption at 1725 cm^{-1}).

The preceding alcohol was dehydrated by dissolving it in benzene and heating under reflux with a bit of p-toluenesulfonic acid collecting the water in a Dean-Stark trap. The dehydration product was fractionally distilled. The olefinic product was collected at $47°$ C. (2.3 mm.) - $52°$ C. (2.0 mm.). The yield was 9.1 g. (16.8%). The IR spectrum was consistent with the desired product (λ $_{max.}$: 1650 cm^{-1} (C=C); 1180 cm^{-1} (C-C); 3500 cm^{-1}, 720 cm^{-1}, 1190 cm^{-1}, 1450 cm^{-1}, and 3000 cm^{-1} (C-H); 1360 cm^{-1} and 1380 cm^{-1} (Gem-dimethyl).

ATTEMPTED SYNTHESIS OF 3,7,7-TRIMETHYL-2-ETHYL-6-TRIPHENYLMETHYL-1,3,5-

CYCLOHEPTATRIENE: Freshly prepared triphenylmethyl perchlorate (23.4 g., 69.4 mmoles) was suspended in 181 ml. of acetonitrile. The material assumed to be 3,7,7-trimethyl-2-ethyl-1,3,5-cycloheptatriene (9.1 g., 56.2 mmoles) was added. The suspension immediately became darker, and the reaction flask became very warm. The triphenylmethyl perchlorate dissolved, but no product precipitated even on standing overnight. When the solution was evaporated to about three-fourths of its original volume, white crystals began to form. These crystals were collected by filtration and washed with acetoni- trile. The yield was 10.13 g. (33%). The product had a melting point of 191-193° C. and an IR spectrum consistent with that expected for N-(5-tri- phenylmethyl-1-ethyl-2,6,6-trimethylcyclohepta-1,3-dien-7-yl)-acetonitrilium perchlorate (λ_{max}^{KBr}: 1493 cm^{-1}, 1600 cm^{-1}, 710 cm^{-1}, 750 cm^{-1}, 770 cm^{-1} (triphenylmethyl); 1450 cm^{-1}, 1375 cm^{-1}, 1390 cm^{-1} (gem-dimethyl); 1690 (C≡N); 1650 cm^{-1} (C=C); and 1025-1125 cm^{-1} (perchlorate ion).

Sodium hydride (2.2 g., 91.7 mmoles) and a bit of sodium borohydride were placed in a 300 ml. round-bottomed flask with about 60 ml. of freshly distilled and dried glyme. A suspension of 5.06 g. of the nitrilium per- chlorate in glyme was dropped into the hydride solution with stirring. The mixture was heated to 85° C. for about two hours. Water was then added to hydrolyze excess sodium hydride, and dilute hydrochloric acid was added to hydrolyze the sodium borohydride and any salts present. The solution was evaporated until a precipitate formed. The yield for the reaction was quantitative. The product had a melting point of 132-134° C. λ_{max}^{KBr}: 3350 cm^{-1}, 1625 cm^{-1} (amine); 705 cm^{-1}, 735 cm^{-1}, 755 cm^{-1}, 1498 cm^{-1}, 1680 cm^{-1} (triphenylmethyl); 1375 cm^{-1}, 1390 cm^{-1} (gem-dimethyl).

The above product, assumed to be ethyl (5-triphenylmethyl-1-ethyl-2,6,6-trimethylcyclohepta-1,3-dien-7-yl) amine (10.5 g., 23.4 mmoles), and methyl iodide (13.3 g., 93.7 mmoles) were dissolved in methyl ethyl ketone and stirred at room temperature for about three hours. The reaction mixture became solid with a yellow precipitate. The yield was 13.1 g. (93%); the melting point was 155-158° C. The crystals gave a positive test for halogen using silver nitrate solution.

The above iodide salt (6.5 g., 11 mmoles) was dissolved in an 8:1 methanol and water mixture. A slurry of silver oxide (5.0 g., 46 mmoles) in methanol was added, and the mixture was stirred vigorously at room temperature for 1.5 hours. A very dark solution formed which was rapidly filtered with suction and placed in a flask for distillation. The distillation system was flushed with nitrogen. The methanol-water solvent was removed under vacuum, and the residue heated at 100° C. (15-25 mm.). The solid became dark and tarry with no indication of elimination occurring. The product was taken up in ether and run through an alumina column giving a clear solution. The ether was evaporated leaving a yellow gummy material which appeared to be polymeric.

The preceding synthesis was repeated. The reaction was run with 5.0 g. of silver oxide and 3.0 g. of the quaternary ammonium iodide for 22 hours. The solution obtained was distilled as before, and the solid residue was heated at 80° C. for about 45 minutes. The tarry product was dissolved in ether leaving behind all insoluble materials. The ether solution was evaporated leaving a tarry yellow-brown material which appeared polymeric. The IR spectrum was made up of broad poorly-defined peaks. It was concluded that none of the desired product was formed.

ATTEMPTED SYNTHESIS OF 3-2-TRIPHENYLMETHYLCAREN-5-ONE: A suspension of
11.1 g. (235 mmoles) of sodamide in 400 ml. of purified dioxane was refluxed
with 25 g. (117 mmoles) of eucarvone under nitrogen. The reaction mixture
was cooled, and 79.3 g. (285 mmoles) of triphenylmethyl chloride were added
all at once to the cool solution. The mixture was then heated under reflux
for one hour and filtered. The dioxane solution was evaporated to about
one-half its original volume, and the product separated as an oil which
settled to the bottom of the flask. The oil was dissolved in ethanol and a
bit of benzene. After several days of refrigeration the dissolved material
began to crystallize. The IR spectrum of the crystalline product did not
show the expected carbonyl absorption and was consistent with that expected
for eucarvone enol triphenylmethyl ether. The material melted at 78-80° C.

A Grignard reaction was attempted with the crystalline solid and methyl
magnesium iodide. Only starting material was recovered from the mixture after
work-up.

The suspected eucarvone enol triphenylmethyl ether (2.5 g.) was
recrystallized from Skelly B solvent. The material dissolved slowly with
warming to about 50-60° C. The solution was cooled with dry ice-acetone.
The crystals obtained showed a rise in melting point to 181-185° C. which
was consistent with the value reported for the bicyclic ketone. The IR
spectrum of the compound was identical with the one reported for the bicyclic
ketone.

A sample (3.0 g.) of the suspected enol ether was recrystallized from
ethanol and a bit of benzene. Warming to 60-70° C. was required, and the
solution was cooled overnight in a refrigerator. The crystals obtained
melted at 81.5-83.5° C. Repeated recrystallizations gave crystals which
melted at 82.0-82.5° C. It was found that wthyl triphenylmethyl ether had

a melting point of 82° C. A sample of this ether was prepared from 10 g. (35.9 mmoles) of triphenylmethyl chloride and 2.4 g. (35.3 mmoles) of sodium ethoxide. Dissolved in 200 ml. of anhydrous ethyl ether, these compounds were heated under reflux for eight hours. The ether was evaporated giving crystalline ethyl triphenylmethyl ether. This compound gave an IR spectrum which was identical with that of the material from the ethanol recrystallization. A mixed melting point was taken with the two materials. The melting point showed no depression. It was concluded that during the recrystallization, the triphenylmethyl ion was trapped by the solvent forming ethyl triphenylmethyl ether and eucarvone. This was further evidenced by the characteristic odor of eucarvone observed during the recrystallization. No further work was attempted on the synthesis.

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HIGHLY SUBSTITUTED CYCLOHEPTATRIENE DERIVATIVES

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AN ABSTRACT OF A THESIS

submitted in partial fulfillment of the

requirements for the degree

MASTER OF SCIENCE

Department of Chemistry

KANSAS STATE UNIVERSITY
Manhattan, Kansas

1967

The synthesis of a series of pentaalkyl tropilidenes was attempted to determine the effect of loading the molecule on the planarity of the ring system.

It was proposed that 2,3,4,7,7-pentasubstituted tropilidenes could be synthesized from eucarvone by the 1,4-addition of a Grignard reagent, a normal Grignard addition and dehydration of the resulting alcohol, allylic bromination, and dehydrobromination. This sequence was found to give in low yields 2,3,7,7-tetramethyl-4-t-butylcycloheptatriene, 3,7,7-trimethyl-2-ethyl-4-t-butylcycloheptatriene, 3,7,7-heptatriene, 3,7,7-trimethyl-2-ethyl-4-t-butylcycloheptatriene, 3,7,7-trimethyl-2,4-di-t-butylcyclohepta-triene, 2,3,7,7-tatramethyl-4-isopropylcycloheptatriene, and 3,7,7-tri-methyl-2-ethyl-4-isopropylcycloheptatriene. The syntheses of 3,7,7-trimethyl-2-isopropyl-4-t-butylcycloheptatriene, 3,7,7-trimethyl-2,4-diisopropylcycloheptatriene, and 3,7,7-trimethyl-2-t-butyl-4-isopropyl-cycloheptatriene failed in the dehydration step. No explanation is apparent for this failure.

Difficulty was encountered in the allylic brominations, also. Equimolar amounts of diene and N-bromosuccinimide were used, and the N-bromosuccinimide reacted quantitatively. However, a considerable amount of addition to double bonds probably occurred. Small amounts of the dienes were recovered along with some of the trienes and large amounts of a very dark, higher-boiling liquid.

When concentrated sulfuric acid and glacial acetic acid were used as a dehydrating agent, four compounds were obtained in equal amounts which were proposed to be isomeric transannular ethers. Infrared spectra, retention times in vapor phase chromatography, and analysis gave confirma-tion to the proposed structures.

In the dehydration of those compounds with a $\underline{t}$-butyl group in the four-position, it appears that the $\underline{t}$-butyl group was lost giving 2,6,6-trimethyl-1-alkylcyclohept-3-enol. The elemental analysis was in agreement with such a structure.

During the conjugate addition of the $\underline{t}$-butyl Grignard reagent to eucarvone, the eucarvone dimer, dieucarvelone, was formed. This product was confirmed by the infrared spectrum, melting point, and elemental analysis.

It was proposed that the 2,3,5,7,7-pentasubstituted tropilidenes could be synthesized by the addition of triphenylmethyl chloride to the sodium salt of eucarvone followed by a normal Grignard addition and dehydration. The expected 3,7,7-trimethyl-5-triphenylmethylbicyclo-[4.1.0] hept-3-en-2-one was not obtained in the first step of the sequence. Instead, the very unstable eucarvone enol triphenylmethyl ether was formed which reacted with solvent in the work-up procedure to give eucarvone and ethyl triphenylmethyl ether.

The proposed synthetic scheme for the 2,3,6,7,7-pentasubstituted tropilidenes involves first the synthesis of 2,3,7,7-tetrasubstituted tropilidenes from eucarvone by normal Grignard addition followed by dehydration. This compound was reacted with triphenylmethyl perchlorate and acetonitrile to give N-(5-triphenylmethyl-1-alkyl-2,6,6,-trimethyl-cyclohepta-1,3-dien-7-yl)-acetonitrilium perchlorate. The nitrilium salt was reduced and a Hofmann elimination was proposed for the resulting amine. The sequence proceeded through the initial stages quite well. However, the final Hofmann elimination failed to give the desired products.

The initial goal of the synthesis and structural analysis of a series of highly substituted tropilidenes was not attained. However, the exploratory work has provided some interesting results and serves as a basis for future work in this general area.